PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHOR	ITY		MANSI				
То:		PCT PCT					
,		WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY					
			(PCT Rule 43bis.1)				
		Date of mailing (day/month/year)	See form PCT/ISA/210				
Applicant's or agent's file reference		FOR FURTHER A	CTION				
P1437PC00			See paragraph 2 below				
International application No.	International filing date (day/month/year)	Priority date (day/month/year)				
PCT/EP2005/003366	24.03.2005	•	24.03.2004				
International Patent Classification (IPC) or both C12Q1/68	n national classification an	dirc	¥ .				
Applicant EPIGENOMICS AG		· ·					
This opinion contains indications rela	ting to the following items	:					
Box No. I Basis of the	opinion						
Box No. II Priority							
Box No. III Non-establi:	shment of opinion with reg	gard to novelty, inventi	ve step and industrial applicability				
Box No. IV Lack of unit	y of invention						
applicability	atement under Rule 43bis. citations and explanation		ovelty, inventive step or industrial ement				
Box No. VI Certain doct	uments cited	·					
Box No. VII Certain defe	ects in the international app	pplication					
Box No. VIII Certain obse	ervations on the internation	nal application	·				
2. FURTHER ACTION							
International Preliminary Examining	Authority ("IPEA") except chosen IPEA has notified	ot that this does not app I the International Bure	l be considered to be a written opinion of the ly where the applicant chooses an Authority other au under Rule 66.1bis(b) that written opinions of				
If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.							
For further options, see Form PCT/IS	A/220.						
3. For further details, see notes to Form	PCT/ISA/220.						
		100000					
Name and mailing address of the ISA/EP		Authorized officer	·				
Facsimile No.		Telephone No.					

Box	No. I Busis of this opinion
1.	With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
	This opinion has been established on the basis of a translation from the original language into the following language
	, which is the language of a translation furnished for the purposes of international search (under
	Rule 12.3 and 23.1(b)).
2.	With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
ľ	a. type of material
	a sequence listing
	table(s) related to the sequence listing
	b. format of material
	in written format
	in computer readable form
	c. time of filing/furnishing
	contained in the international application as filed.
	filed together with the international application in computer readable form.
	furnished subsequently to this Authority for the purposes of search.
3. 4.	In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. Additional comments:
, ·	Auditorial conflictes.
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Box No. II Priority	_
1. The following document has not yet been furnished:	1
copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).	1
translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).	-
Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established the assumption that the relevant date in the claimed priority date.	n
2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found inval (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.	d ie
3. Additional observations, if necessary:	
The validity of the priority claim has not been	
considered because the International Searching Authority	
does not have in its possession a copy of the earlier	
application whose priority has been claimed or, where	
required, a translation of that earlier application. This	
opinion has nevertheless been established on the	
assumption that the relevant date (Rules 43bis1 and 64.1)	
is the claimed priority date.	
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Box	No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to not citations and explanations supporting such statement	velty, inventive step or industrial applicability;
1.	Statement		
	Novelty	(N) Claims 1-22	YES
			NO NO
	Inventiv	re step (IS) Claims 1-22	YES
			NO.
	Industria	al applicability (IA) Claims 1-22	YES
			NO
	.,		
2.	Citations an	ad explanations:	
	1)	Reference is made to the follo	owing documents:
		D1: COTTRELL S E ET AL: "A re	val-time PCR assav
		for DNA-methylation using	
		specific blockers" NUCLEI	
		OXFORD UNIVERSITY PRESS,	
		no. 1, 13 January 2004 (2	
		,	.004-01 13/, page
		e10.	LI NI V. DETMAN
		D2: WO 02/070735 A (AKZO NOBE	
		BIRGIT, ALBERTA, LOUISA,	
		INGE) 12 September 2002 (
		D3: WO 97/47762 A (SARNOFF CC	
		December 1997 (1997-12-18	3) •
	2)	Document D1 is considered the	prior art closest to
	2)	the subject matter of claim 1.	
		method of analyzing DNA methyl	•
		bisulfite conversion of the DN	
		methylated cytosine bases being	
		uracil while 5-methylcytosine	
		unchanged. Subsequent use of b	
		oligonucleotides results in an	increase in PCK
		amplification specificity.	

International application No.
PCT/EP2005/003366

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The subject matter of the application differs from that of D1 in that the method includes a transcription-based amplification step. The subject matter of the application is therefore novel over D1 (PCT Article 33(2)).

with respect to D1, the problem addressed by the present invention can be considered that of providing an improved DNA methylation analysis. The application solves this problem by using a transcription-based amplification step in the claimed method. Documents D2 and D3 have previously disclosed methods of amplifying DNA by using a transcription-based amplification. However, non of the documents D1 to D3 includes any indication of combining the method of D1 with the transcription-based amplification according to D2 and/or D3. For this reason, the claimed subject matter of protection appears to involve an inventive step (PCT Article 33(3)).

Certain published documents (Rule 43 <i>bis</i> . 1 and 7 Application No. Patent No.	(0.10) Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid clain (day/month/year)
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Non-written disclosures (Rule 43bis.1 and 70.9)			
Non-written disclosures (Rule 43bis.1 and 70.9) Kind of non-written disclosure	Date of non-written di (day/month/yea	sclosure referrin	e of written disclosure g to non-written disclosure (day/month/year)
		sclosure referrin	g to non-written disclosure
		sclosure referrin	g to non-written disclosure
		sclosure referrin	g to non-written disclosure
		sclosure referrin	g to non-written disclosure
		sclosure referrin	g to non-written disclosure
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Kind of non-written disclosure		sclosure referrin	g to non-written disclosure
Kind of non-written disclosure		sclosure referrin	g to non-written disclosure
Kind of non-written disclosure		sclosure referrin	g to non-written disclosure

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHO	ORITY		'VS'
То:			PCT PCT
			RITTEN OPINION OF THE IONAL SEARCHING AUTHORITY
			(PCT Rule 43bis.1)
		Date of mailing (day/month/year)	See form PCT/ISA/210
Applicant's or agent's file reference		FOR FURTHER	ACTION
P1437PC00			See paragraph 2 below
International application No.	International filing date	(day/month/year)	Priority date (day/month/year)
PCT/EP2005/003366	24.03.2005		24.03.2004
International Patent Classification (IPC) or b	oth national classification an	nd IPC	
C12Q1/68			
Applicant	•		
EPIGENOMICS AG			,
This opinion contains indications in	elating to the following item	s:	
abla			
	the opinion		
Box No. II Priority		10.00	the state of the desired months while to
	•	gard to noverty, invent	ive step and industrial applicability
	unity of invention	. M. N	- coulty inventive cten or industrial
Box No. V Reasone applicab	d statement under Rule 43 <i>018</i> ility; citations and explanatio	ons supporting such sta	novelty, inventive step or industrial tement
Box No. VI Certain o	locuments cited		
Box No. VII Certain o	defects in the international ap	plication	
Box No. VIII Certain	observations on the internation	onal application	
2. FURTHER ACTION			
International Preliminary Examini than this one to be the IPEA and this International Searching Author	ing Authority ("IPEA") except the chosen IPEA has notified the rity will not be so considered	pt that this does not ap d the International Bu d.	Il be considered to be a written opinion of the ply where the applicant chooses an Authority other reau under Rule 66.1bis(b) that written opinions of
If this opinion is, as provided abo written reply together, where ap PCT/ISA/220 or before the expira	propriate, with amendments	, before the expiration	A, the applicant is invited to submit to the IPEA and of 3 months from the date of mailing of Form expires later.
For further options, see Form PC1	YIS A/220.		
3. For further details, see notes to Fo	rm PCT/ISA/220.		
Name and mailing address of the ICA/RD		Authorized officer	
Name and mailing address of the ISA/EP			

Facsimile No.

Box	No. I		Busis of this o	pinion								
1.			to the language otherwise indica			established or	the basis	of the interna	ational app	olication in th	e language in	which it was
		This o	pinion has been	cstablished (
					, which i	s the language	of a trans	lation furnish	ed for the	purposes of i	nternational s	carch (under
		Rule 1	2.3 and 23.1(b))									
2.			to any nucleo is opinion has b				disclosed i	n the interna	ational ap	plication and	necessary to	the claimed
	a.	type of	material									
	· [sequence listin	g								
		[] t	able(s) related to	the sequen	ce listing							
	ь.	format	of material					•				
		⊠ i	n written format			•						
		⊠ i	n computer read	lable form								
	c.	time of	f filing/furnishin	ıg								
	1	\Box	ontained in the	international	application	as filed.						
	ĺ	\sqcap ,	iled together wi	th the interna	ational appl	ication in com	puter read	able form.				
			urnished subseq				-					
	1	٠ لحكا		,		and hambar						
3.	_	furnish	ition, in the cas led, the required r does not go be	statements	that the info	ormation in th	e subseque	nt or additio				
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4.	Vaait	tionalc	omments:					÷				
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Box !	No. II Priority
1.	The following document has not yet been furnished:
	copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
	translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).
	Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date in the claimed priority date.
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	Additional observations, if necessary:
	The validity of the priority claim has not been
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	does not have in its possession a copy of the earlier
	application whose priority has been claimed or, where
	required, a translation of that earlier application. This
-	opinion has nevertheless been established on the
	assumption that the relevant date (Rules 43bis1 and 64.1)
•	is the claimed priority date.
	\cdot

Box	No. V				alc 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; porting such statement	
1.	Statement					
	Novelty	(N)		Claims	1-22	YES
				Claims		МО
	Inventiv	e step (IS)		Claims	1-22	YES
				Claims		NO
	· Industria	al applicabil	ity (IA)	Claims	1-22	YES
				Claims		NO
2.	Citations an	d explanatio	ons:			· · · · · · · · · · · · · · · · · · ·
	1)	•		is m	ade to the following documents:	
	-,			20 1		•
		D1:	COTTE	RELL :	S E ET AL: "A real-time PCR assay	
					ethylation using methylation-	
					blockers" NUCLEIC ACIDS RESEARCH,	
			-		IVERSITY PRESS, SURREY, GB, vol. 32,	
					January 2004 (2004-01-13), page	
			e10.	·	•	
		D2:	WO 02	2/070	735 A (AKZO NOBEL N.V; DEIMAN,	
			BIRG	T, A	LBERTA, LOUISA, MARIA; FRANTZEN,	
			INGE)	12	September 2002 (2002-09-12).	
		D3:	WO 97	7/477	62 A (SARNOFF CORPORATION) 18	
			Decer	mber	1997 (1997-12-18).	
	2)	Docu	ment I)1 is	considered the prior art closest to	
		the :	subje	ct ma	tter of claim 1. It discloses a	
		meth	od of	anal	yzing DNA methylation, comprising	
		bisu.	lfite	conv	ersion of the DNA, with any non-	
		meth	ylated	d cyt	osine bases being converted to	
		urac	il whi	lle 5	-methylcytosine bases remain	
		unch	anged.	Sub	sequent use of blocker	
		olig	onucle	eotid	es results in an increase in PCR	
		ampl	ificat	ion :	specificity.	

International application No.
PCT/EP2005/003366

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

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Box	No. VI	Certain documents cited	ı			
1.	Certain pu	ublished documents (Rule 43bi	s.1 and 70.10))		
		Application No. Patent No.		Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
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2.	Non-writte	en disclosures (Rule 43bis.1 an	ıd 70.9)			Follows:
	_	Kind of non-written disclosur	re	Date of non-written dia (day/month/year	sclosure referri	hate of written disclosure ing to non-written disclosure (day/month/year)
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